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DESIGNATED/ELECTED OFFI CONCERNING A FILING UNDE	CE (DO/EO/US)	U.S. APPLICATION NO. (if knoft) = 917 CF8.568379
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INTERNATIONAL APPLICATION NO. PCT/EP99/09683	INTERNATIONAL FILING DATE December 9, 1999	PRIORITY DATE CLAIMED December 18, 1998
TITLE OF INVENTION FINE SUSPENSIONS OF PO CARE PRODUCTS	OORLY SOLUBLE CALCIUN	I SALTS AND THEIR USE IN DENTAL
APPLICANT(S) FOR DO/EO/US Christian KROPF, Ulrike B WUELKNITZ, Rolf HEMPEL	RUENINGHAUS, Amergio P MANN and Marcel ROTH	ASTURA, Michael MEINDERS, Peter
Applicant herewith submits to the United Sta	ites Designated/Elected Office (EO/DO/US) to	ne following items and other information:
1. This is a FIRST submission of ite	ms concerning a filing under 35 U.S.C. 371.	
2. This a SECOND or SUBSEQUE	NT submission of items concerning a filing und	der 35 U.S.C. 371.
3. This express request to begin nat examination until the expiration of	ional examination procedures (35 U.S.C. 371) the applicable time limit set in 35 U.S.C. 371(f)) at any time rather than delay b) and PCT Articles 22 and 39 (1).
4. M A proper Demand for Internationa	I Preliminary Examination was made by the 19	th month from the earliest claimed priority date.
5. A copy of the International Application	ation as filed (35 U.S. C. 371(c)(2)). Equired only if not transmitted by the Internation	nal Bureau).
b. a has been transmitted by t		•
6. A translation of the International App	lication into English (35 U.S.C. 371(c)(2)).	
a. are transmitted herewith (b. have been transmitted by	ever, the time limit for making such amendme	onal Bureau).
	he claims under PCT Article 19 (35 U.S.C. 3	71(c)(3)).
9. An oath or declaration of the inventor	r(s) (35 U.S.C. 371(c)(4)).	
10. \square A translation of the annexes to the Ir	nternational Preliminary Examination Report un	der PCT Article 36 (35 U.S.C. 371(c)(5)).
Items 11. to 16. below concern other doc 11. An Information Disclosure Statemen		
12. □ An assignment document for record	ing. A separate cover sheet in compliance wit	h 37 CFR 3.28 and 3.31 is included.
13. ■ A FIRST preliminary amendment □ A SECOND or SUBSEQUENT prei	iminary amendment.	
14. □ A substitute specification.		
15. □ A change of power of attorney and/o	r address letter.	
16. ☐ Other items or information.:		
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PATENT
Docket H 3763 PCT/US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re: PCT/EP99/09683

International Filing Date: December 9, 1999

Priority Date:

December 18, 1998

Applicant:

KROPF, et al.

Title:

FINE SUSPENSIONS OF POORLY

SOLUBLE CALCIUM SALTS AND THEIR

USE IN DENTAL CARE PRODUCTS

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents Washington, DC 20231

Please enter the amendments below before examining this case on the merits:

IN THE SPECIFICATION:

On page 1, insert below the title:

-- CROSS-REFERENCE TO RELATED APPLICATIONS

This application is the U.S. National Stage application filed under 35 U.S.C. § 371 of International Application No. PCT/EP99/09683, filed December 9, 1999, in the European Patent Office, claiming priority under 35 U.S.C. §§ 119 and 365 of PCT/EP99/09683 and DE 198 58 662.0, filed on December 18, 1998, in the German Patent Office.—

On page 3, after line 30, insert the heading -- DESCRIPTION OF THE INVENTION--.

IN THE CLAIMS:

Please cancel claims 1 to 7 without prejudice, and add new claims 8 to 14:

- 8. A suspension of one or more phosphate, fluoride, or fluorophosphate calcium salts in a liquid medium in which the salts are less than 1 g/l soluble, wherein the calcium salts comprise primary particles having diameters of from 5 to 50 nanometers and lengths of from 10 to 150 nanometers, stabilized against agglomeration by a content of at least 0.01% by weight, based on the weight of the suspension, of a water-soluble surfactant or of a water-soluble polymeric protective colloid.
- 9. The suspension of claim 8, comprising 1% to 40% by weight of the one or more calcium salts and 0.1% to 10% by weight, based on the weight of the one or more calcium salts, of the water-soluble surfactant or the water-soluble polymeric protective colloid.
- 10. The suspension of claim 9, comprising 1% to 10% by weight, based on the weight of the one or more calcium salts, of one or more nonionic surfactants.
- 11. A process for the preparation a suspension of poorly soluble calcium salts, comprising the steps of precipitating one or more phosphate, fluoride, or fluorophosphate calcium salts in an aqueous medium in which these salts are less than 1 g/l soluble, wherein the calcium salts comprise primary particles having diameters of from 5 to 50 nanometers and lengths of from 10 to 150 nanometers, said precipitation being carried out in the presence of water-

soluble surfactants or water-soluble polymeric protective colloids.

- 12. The process of claim 11, wherein the aqueous medium is an acidic solution of a water-soluble calcium salt and a stoichiometric amount of a water-soluble phosphate salt with a pH below 3, and the precipitation is effected by increasing the pH using aqueous alkalis or ammonia in the presence of the water-soluble surfactants or water-soluble polymeric protective colloids.
- 13. A toothpaste comprising one or more silica polishing agents, humectants, binders or aromas and 0.1-5% by weight of one or more calcium salts selected from the group consisting of amorphous calcium phosphate, hydroxylapatite, fluorapatite, and calcium fluoride, said calcium salts being present in the form of a suspension of one or more of the salts in a liquid medium in which the salts are less than 1 g/l soluble, wherein the salts comprise primary particles having diameters of from 5 to 50 nanometers and lengths of from 10 to 150 nanometers, stabilized against agglomeration by a content of at least 0.01% by weight, based on the weight of the suspension, of a water-soluble surfactant or of a water-soluble polymeric protective colloid.
- 14. A method of remineralizing teeth comprising the steps of applying to a tooth a remineralizing-effective amount of a suspension of one or more phosphate, fluoride, or fluorophosphate calcium salts in a liquid medium in which the salts are less than 1 g/l soluble, wherein the calcium salts comprise primary particles having diameters of from 5 to 50 nanometers and lengths of from 10 to 150 nanometers, stabilized against agglomeration by a content of at least

0.01% by weight, based on the weight of the suspension, of a water-soluble surfactant or of a water-soluble polymeric protective colloid.

REMARKS

Claims 1-7 have been canceled without prejudice, and new claims 8-14 added. The subject matter of the new claims is described in the specification at page 3, line 32 to page 4, line 12, page 7, lne 19, to page 8, line 4, page 8, lines 17-26, and page 10, lines 4-9, as well as in the claims as originally filed. The specification has been amended to include a cross-reference to related applications and headings appropriate to U.S. practice. No new matter has been added.

The new claims better claim the full literal and equivalent scope and breadth of subject matter disclosed in the application, notwithstanding applicants' belief that the original claims, drafted for examination in the German and European Patent Offices, would have been allowable but for minor matters of form permitted in German or European practice but objected to in the U.S.P.T.O. The new claims find support in the application independent of the original claims and therefore are not believed to constitute narrowing amendments to the original claims within the holding of Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., No. 95-1066 (Fed. Cir. Nov. 29, 2000).

Applicants respectfully request entry of this Amendment and examination of the application. If any fees are due to enter this paper that have not been accounted for, please charge Deposit Account No. 01-1250.

Respectfully submitted,

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WO 00/37033

H 3763 PCT/EP99/09683

Patent Application

"Fine suspensions of poorly soluble calcium salts and their use in dental care products"

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invention relates to fine suspensions of poorly soluble calcium salts which, because of their particle size in the nanometer range and their stability toward agglomeration, are particularly suitable dental care products.

Phosphate salts of calcium have for a long time been either as abrasive components orto promote remineralization of tooth enamel to formulations dental cleaning products and dental care products. This true particularly for hydroxylapatite fluorapatite, and for amorphous calcium phosphates and for brushite (dicalcium phosphate dihydrate). However, calcium fluoride has also been described a number of times as a constituent of dental cleaning products and as a component for strengthening tooth enamel and for the prophylaxis of caries.

The availability of these substances for the desired 25 remineralization depends quite decisively on the particle size of these poorly water-soluble components dispersed in the dental care products. It has therefore been proposed to use these poorly soluble calcium salts in extremely fine dispersion.

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DE-A-2134862 discloses, for example, a dental care product for hypersensitive teeth which comprises hydroxylapatite $(Ca_5[(PO_4)_3OH])$ divided particle size, however, is given as 6-8 µm (micrometers) since greater finenesses cannot be achieved by grinding.

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Dental care products comprising separate components have also already been proposed, of which one comprises a dissolved Ca salt and the other comprises a dissolved phosphate or fluoride salt, and which are combined only shortly prior to application - or which are used in succession - in order to apply the freshly precipitated and still amorphous or finely crystalline calcium salts to the tooth surface. The disadvantages of such handling are obvious since the user has to use two products successively or combine them shortly before use. compositions which comprise freshly precipitated, still amorphous calcium phosphates or calcium fluoride are stored, the precipitates age, the crystallites grow and agglomerate to give coarser secondary particles. This reduces the remineralizing action and jeopardizes the stability of the dispersion.

The object was therefore to provide suspensions of such poorly soluble calcium salts whose particle size is in the nanometer range and which are largely protected against agglomeration.

WO 94/04460 Al describes a process for the preparation of amorphous calcium salts and their use the remineralization of teeth. EP 786245 Al describes dental products which comprise hydroxylapatite having particle sizes of from 0.05 to 1.0 μm which are obtained WO 98/18719 discloses a hydroxylapatite by grinding. composition which comprises hydroxylapatite with particle diameters of 10-20 nm and particle lengths of 50-100 nm and which are intended to be used, for example, toothpastes. These are obtained by concentrating very dilute suspensions by two or more filtration steps.

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EP 0499299 A2 discloses suspensions of particles crystalline drugs which have a size of less than 100 nm contain, adsorbed on their surface, a modifier which may also be a surfactant or a polymeric protective colloid. Stabilization of inorganic poorly soluble salts obtained by precipitation reactions is not disclosed. WO 96/34829 Al discloses a process for little-agglomerated particles preparation of the nanometer range, in which a suspension of such particles is prepared from the precursors in a liquid medium which has no noteworthy solvency for the particles, presence of a surface-blocking substance. In another embodiment, a sol which comprises amorphous or partially crystalline nanoparticles is suspended in the presence of the surface-blocking substance. Also named as surfaceblocking substances are (poly) carboxylic acids nonionogenic surfactants. Disclosed as suitable particles are, however, only oxide (hydrates), sulfides, selenides, tellurides and phosphides precipitated from hydrolyzable salts or organometallic compounds by adding water or changing the pH. Phosphates or fluorides of calcium or use of the suspensions in dental care products are not disclosed.

It has now been found that suspensions of poorly watersoluble calcium salts in very finely divided form can be stabilized during the precipitation or shortly thereafter if the precipitation is carried out in the presence of an agglomeration inhibitor, or the dispersion is redispersed in the presence of the agglomeration inhibitor.

The invention therefore provides a suspension of poorly water-soluble calcium salts, chosen from phosphates, fluorides and fluorophosphates, in a liquid medium in which these calcium salts are insoluble or poorly

soluble, characterized in that the calcium salts are present in the form of primary particles having diameters of from 5 to 50 nanometers and lengths of from 10 to 150 nanometers and are stabilized against agglomerization by a content of at least 0.01% by weight, based on the weight of the suspension, of a water-soluble surfactant or of a water-soluble polymeric protective colloid.

Poorly soluble or poorly water-soluble salts are to be understood as meaning those salts which are soluble in water or in the liquid suspension medium to an amount of less than 1 g/l (20°C). Suitable salts are preferably calcium hydroxyphosphate ($Ca_5[OH(PO_4)_3]$) or hydroxylapatite, calcium fluorophosphate, ($Ca_5[F(PO_4)_3]$) or fluorapatite, F-doped hydroxylapatite of the general composition $Ca_3(PO_4)_3(OH,F)$ and calcium fluoride (CaF_2) or fluorite (fluorspar).

A suitable liquid medium in which the calcium salts can be dispersed is primarily water. However, the calcium salt particles isolated from an aqueous suspension, e.g. by filtration or centrifugation, can also be redispersed in organic solvents and, in this case, likewise produce suspensions of the primary particles in the nanometer range which have virtually no tendency for agglomeration. Suitable organic liquid media are, for example, watersoluble, lower alcohols and glycols, polyethylene glycols, glycerol or mixtures thereof with one another or with water.

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Primary particles are understood here as meaning the crystallites, i.e. the individual crystals, of said calcium salts. The particle diameter should be understood here as meaning the smallest diameter, and the length to be understood as meaning the greatest diameter of the

crystal particles, e.g. the length of a rod-shaped crystallite. Wherever an average particle diameter is discussed, this is understood as meaning a volume-averaged value.

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For the purposes of the present invention, water-soluble surfactants are understood as meaning all surface-active lipophilic by a characterized substances alkylphenyl or acyl radical having 8-22 carbon atoms and a hydrophilic, ionic or nonionic group which imparts to the surfactant a solubility in water of more than 1 g/l (20°C). Suitable as anionic surfactants are, for example, salts of C₈-C_{1.8}ammonium metal or the alkali alkanecarboxylic acids (soaps), of alkyl- $(C_{12}-C_{18})$ sulfuric monoesters (alkyl sulfates), of alkylpolyglycol ether sulfuric monoesters (ether sulfates), of sulfosuccinic (sulfosuccinates), mono-C₈-C₁₈-alkyl esters alkanesulfonic acids (alkanesulfonates), of C12-C18acyloxyethanesulfonic acids (isethionates), of C_{12} - C_{18} acylaminoalkanesulfonic acids (taurides), of $N-C_{12}-C_{18}-$ (sarcosinates), of alkylpolyglycol acylsarcosine carboxylates), of (ether carboxylic acids phosphoric acids ether) alkyl(polyglycol (alkyl(polyglycol ether) phosphate).

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are, for example, Suitable cationic surfactants alkyldimethylbenzylchloride, alkyltrimethylammonium alkylpyridinium chloride, chloride, ammonium chloride. alkyldimethylhydroxyethylammonium and acylimidazolinium methosulfates acyloxyethyltrimethylammonium chloride.

Suitable zwitterionic surfactants are, for example, betaine surfactants, such as, for example,

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alkyldimethylcarboxymethylbetaine acylaminoalkyldimethylcarboxymethylbetaine.

and

Amphoteric surfactants, such as, for example, alkylaminopropanecarboxylic acids, are also suitable as ionic surfactants.

surfactants are nonionic However, the suitable, in particular the addition products of ethylene oxide to lipids with mobile hydrogen atoms. Such suitable the addition nonionic surfactants are, for example, products of 6-60 mol of ethylene oxide to linear fatty alcohols, to fatty acids, to fatty amines, to fatty acid monoglycerides, to sorbitan fatty acid monoesters, fatty acid monoesters, sugar to alkylphenols, methylglucoside fatty acid monoesters and to fatty acid monoethanolamides. Further preferably suitable nonionic surfactants are the alkyl (oligo) glucosides obtainable by reacting glucose with C_8 - C_{18} -fatty alcohols or by transacetylation of butyl(oligo) glucoside with fatty alcohols. Preferably suitable alkyl (oligo) glucosides are, for example, the alkyl (C_8-C_{16}) glucosides having average degrees of oligomerization (of the glucoside radical) of from 1 to 2. Such products are [lacuna] commercially, e.g. under the trade name Plantacare® 1200 suitable preferably Plantacare® 600. Further nonionogenic surfactants are the mixtures obtainable by castor oil which hydrogenated ethoxylation of obtained, for example, by the addition of 30, 40 or 60 mol of ethylene oxide to hydrogenated castor oil.

Finally, amine oxide surfactants and sugar fatty acid esters are also suitable as nonionogenic surfactants.

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colloids protective polymeric Water-soluble understood as meaning high molecular weight compounds which are adsorbed on the surface of the nanoparticles and modify these such that they are hindered from polymeric agglomerating. Suitable coagulating and protective colloids are, for example, natural watersoluble polymers, such as, for example, gelatin, casein, albumin, starch, plant gums and water-soluble derivatives of water-insoluble polymeric natural substances, such as, (methylcellulose, ethers cellulose example, carboxymethylcellulose), hydroxyethylcellulose, hydroxyethylstarch or hydroxypropylguar.

Synthetic water-soluble polymers suitable as protective colloids are, for example, polyvinyl alcohol, polyvinylpyrrolidone, polyacrylic acids, polyaspartic acid and others.

The suspensions according to the invention are prepared by precipitation reactions from aqueous solutions water-soluble calcium salts and aqueous solutions salts. water-soluble phosphate or fluoride precipitation is carried out in the presence of watersoluble surfactants or water-soluble polymeric protective colloids. This may, for example, be carried out by adding the surfactants or protective colloids to the aqueous phosphate or fluoride salt solution or to the solution of the calcium salt prior to the reaction. Alternatively, the aqueous calcium salt solution can be added to an aqueous surfactant or protective colloid solution at the same time as the phosphate or fluoride salt solution.

A further process variant involves the precipitation being carried out from a strongly acidic solution of a water-soluble calcium salt and a stoichiometric amount of a water-soluble phosphate salt with a pH below 3 by increasing the pH using an aqueous alkali or ammonia in the presence of water-soluble surfactants or water-soluble polymeric protective colloids.

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The concentration of poorly soluble calcium salt in the suspensions according to the invention can cover a wide range from about 1 to 40% by weight. Here, the content can be increased on the one hand during the preparation by means of the concentration of the water-soluble salts, and on the other hand after the precipitation reaction by concentration, e.g. by filtration or centrifugation or by distilling off some of the water, without the effect of the surfactant or of the protective colloid being lost in the process.

The concentration of the surfactant or of the polymeric protective colloid in the agueous suspension is, for example, 0.1 to 20% by weight, preferably 0.1-10% by weight, based on the content of poorly soluble calcium salt. In a preferred embodiment, the suspension according to the invention therefore comprises 1-40% by weight of calcium salts and, for poorly soluble stabilization, 0.1-10% by weight of a water-soluble surfactant or of a water-soluble polymeric protective colloid, based on the weight of the calcium salt.

Preferably suitable for the stabilization against agglomeration are predominantly the nonionic surfactants in an amount of from 1 to 10% by weight, based on the weight of the calcium salt. The nonionic surfactants of the type of alkyl C_8 - C_{16} -(oligo)- glucosides and of ethoxylates of hydrogenated castor oil have proven particularly effective. These can also be used together

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with the polymeric protective colloids for the stabilization.

the preparation of suspensions according to the invention in other liquid media, it is expedient to start from aqueous suspensions according to the invention, free these by filtration or centrifugation from the aqueous dry, where appropriate, the nanoparticles redisperse them in organic solvents. Here, addition of surfactants or protective colloids is no longer necessary since the nanoparticles comprise the required for inhibition amounts of stabilizer agglomeration adsorbed on the surface. The finely divided nature and stability of such suspensions is therefore comparable with those of the aqueous suspensions. Another possibility consists in mixing the aqueous suspension with a higher-boiling solvent, e.g. with glycerol, and removing the water by distillation. Suitable as organic liquid medium is, particularly with regard to use in dental care products, primarily glycerol and its liquid mixtures with sorbitol and optionally with water.

The suspensions according to the invention, in particular those of hydroxylapatite, fluorapatite and calcium fluoride, are suitable as remineralizing component for the preparation of compositions for the cleaning and care of teeth. As a result of the particularly finely divided nature, the effect, known per se, of strengthening the tooth enamel and closing lesions and dentinal tubules can take place particularly rapidly and completely. compositions for the cleaning and care of teeth may here in the form of pastes, liquid creams, gels or mouthwashes. Even in liquid preparations, the suspensions according to the invention disperse readily and the

calcium salts remain stably dispersed and do not tend toward sedimentation.

A preferred embodiment are, however, toothpastes with a content of silica, polishing agents, humectants, binders and aromas which comprise 0.1-5% by weight of finely divided calcium salts from the group hydroxylapatite, fluorapatite and calcium fluoride in the form of a suspension according to the invention.

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The preparations for the cleaning and care of teeth can comprise the customary components and auxiliaries of such compositions in the amounts customary for this purpose. For toothpastes, these are, for example,

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- cleaning and polishing substances, such as, for example, chalk, silicas, aluminum hydroxide, aluminum silicates, calcium pyrophosphate, dicalcium phosphate, insoluble sodium metaphosphate or synthetic-resin powder
- humectants, such as, for example, glycerol, 1,2-propylene glycol, sorbitol, xylitol and polyethylene glycols
- binders and consistency regulators, e.g. natural and synthetic water-soluble polymers and water-soluble derivatives of natural substances, e.g. cellulose ethers, phyllosilicates, finely divided silicas (aerogel silicas, pyrogenic silicas)
- aromas, e.g. peppermint oil, spearmint oil, eucalyptus oil, aniseed oil, fennel oil, caraway oil, menthyl acetate, cinnamaldehyde, anethole, vanillin, thymol and mixtures of these and other natural and synthetic aromas
- sweeteners, such as, for example, saccharin-sodium,
 sodium cyclamate, aspartame, acesulfame K, stevioside,

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monellin, glycyrrhicine, dulcin, lactose, maltose or fructose

- preservatives and antimicrobial substances, such as, for example, p-hydroxybenzoates, sodium sorbate, triclosan, hexachlorophene, phenylsalicylates, thymol etc.
- pigments, such as, for example, titanium dioxide or pigment dyes for producing colored stripes
- buffer substances, e.g. primary, secondary or tertiary alkali metal phosphates, citric acid/Na citrate
- wound-healing and antiinflammatory active ingredients, e.g. allantoin, urea, azulene, panthenol, acetylsalicylic acid derivatives, plant extracts, vitamins, e.g. retinol or tocopherol.

The examples below serve to illustrate the subject-matter of the invention in more detail:

Examples

 Preparation of suspensions of poorly soluble calcium salts

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- 1.1 Preparation of a hydroxylapatite suspension by precipitation and redispersion
- 50.86 g of $Ca(NO_3)_2 \cdot 4H_2O$ were dissolved in demin. water and made up to 200 ml. 10 g of Plantacare 1200® were added to this. 60 ml of 25% strength ammonia solution were then added, so that the pH was 12.
- 17 g of ammonium hydrogenphosphate with dissolved in demin. water and made up to 200 ml. 10 g of Plantacare 1200® were added to this. 60 ml of 25% strength ammonia solution were then added.
- Both solutions were brought to 75°C and mixed with vigorous stirring. After stirring for one hour, the precipitate was centrifuged off, washed a number of times with water and then taken up in water to give a 5% strength by weight hydroxylapatite suspension. The particle sizes were 4-10 nm \times 60-130 nm (diameter \times length).

(demin. = demineralized)

25 1.2 Preparation of a hydroxylapatite suspension by reprecipitation (pH shift) and concentration by evaporation

25.43 g of Ca(NO₃)₂·4H₂O were dissolved in demin. water and made up to 100 ml. 8.5 g of ammonium hydrogenphosphate were likewise dissolved in demin. water and made up to 100 ml. The solutions were combined, with formation of a voluminous precipitate. 37% strength hydrochloric acid was added dropwise to the suspension until the precipitate had completely dissolved at pH 2.

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A mixture of 200 ml of demin. water, 200 ml of 25% strength ammonia solution and 20 g of Cremophor RH 60® (BASF, castor oil + 60 EO) was initially introduced. At 0°C, the apatite solution was added dropwise to this solution with stirring, with formation of a precipitate. Excess ammonia was separated off by distillation, then the mixture was washed by means of dialysis until nitrate-free. Concentration by evaporation on a rotary evaporator gave a 10% strength by weight suspension of hydroxylapatite. The particle sizes were 30 nm (volume-averaged) in diameter (determination using a Micro-Trac 3.150 Ultrafine Particle Analyzer 150 by averaging over the total particle volume).

15 1.3 Preparation of a suspension of hydroxylapatite analogously to Example 1.2 (starting from CaCl₂)

11.95 g of calcium chloride were dissolved in demin. water and made up to 100 ml. 7.4 g of ammonium hydrogenphosphate were likewise dissolved in demin. water and made up to 100 ml. The solutions were combined with formation of a voluminous precipitate. 37% strength hydrochloric acid was added dropwise to the suspension until the precipitate had completely dissolved at pH 2.

A mixture of 200 ml of demin. water, 200 ml of 25% strength ammonia solution and 20 g of Cremophor RH 60® (BASF, castor oil + 60 EO) was initially introduced. At 0°C, the apatite solution was added dropwise to this solution with stirring, with formation of a precipitate. Excess ammonia was separated off by distillation, then the mixture was washed by means of dialysis until nitrate-free. Concentration by evaporation on a rotary evaporator gave a 10% strength by weight suspension of hydroxylapatite. The particle sizes were 10-35 nm × 20-50 nm (diameter × length).

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1.4 Preparation of the hydroxylapatite suspension analogously to Example 1.2 using Arlatone 289 (BASF)

Instead of 20 g of Cremophor RH 60, 35 g of Arlatone 289 were used. A 10% strength by weight suspension of hydroxylapatite with an average particle size of 40 nm was obtained. (Micro-Trac 3.150 Ultrafine Particle Analyzer).

1.5 Preparation of a hydroxylapatite suspension in glycerol

0.3 mol of calcium chloride were dissolved in 2000 ml of demin. water and thermostatted at 25°C. Ammonia solution was used to establish a pH of 12. Then, with vigorous of 0.18 mol solution of ammonium stirring, а hydrogenphosphate in 400 ml of demin. water, which was thermostatted at 25°C and had been adjusted to pH 10 using ammonia, was slowly added dropwise. After reaction time of 20 h, 3 g of Cremophor RH 60® solution (40% strength by weight in demin. water) were added and dispersed by inputting chemical energy (stirring, ultrasound). The suspension was then centrifuged off a number of times and washed firstly with 1% strength aqueous Cremophor RH60® solution, then with ethanol. The material was then taken up in 100 ml of Hydroxylapatite particles with sizes of 5-20 nm \times 10-70 nm (diameter x length) were present in this glycerol suspension.

1.6 Preparation of a suspension of fluorine-doped hydroxylapatite in glycerol

0.3 mol of calcium chloride were dissolved in 2000 ml of demin. water and thermostatted at 25°C. Ammonia solution was used to establish a pH of 12. For this, a solution of 2.27 g of ammonium fluoride in 50 ml of demin. water was added. Then, with vigorous stirring, a solution of

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0.18 mol of ammonium hydrogenphosphate in 400 ml of demin. water, which was thermostatted at 25°C and had been adjusted to pH 10 using ammonia, was slowly added dropwise. After a reaction time of 20 h, 3 g of Cremophor RH 60® solution (40% strength by weight in demin. water) were added and dispersed by inputting chemical energy (stirring, ultrasound). The suspension then was centrifuged off a number of times and washed firstly with 1% strength aqueous Cremophor RH60® solution, then with ethanol. The material was then taken up in 100 ml of glycerol. Here, a glycerol suspension of Ca₅(PO₄)₃(OH, F) particles with a size of 5-20 nm \times 10-70 nm (diameter \times length) was obtained.

15 1.7 Preparation of a calcium fluoride suspension by precipitation

11.95 g of anhydrous CaCl₂ were dissolved in demin. water made up to 100 ml. 200 ml of demin. water, 35 g of Arlatone 289 (BASF) and 15 g of ammonium fluoride were mixed in a receiver. Both solutions were cooled to 0°C and the first solution was added to the second with vigorous stirring. The dispersion formed was concentrated by evaporation on a rotary evaporator at 70°C until the solids content was 10% by weight. Washing was then carried out by means of dialysis. This gave a calcium fluoride suspension with an average (volume-weighted) particle size of 20 nm.

2. Dental creams with calcium salt nanoparticles

Formulation examples	2.1	2.2
Sident® 8	10.0% by wt.	10.0% by wt.
Sident® 22S	7.0% by wt.	7.0% by wt.
Sipernat® 320DS	0.8% by wt.	0.8% by wt.
CaF ₂ suspension Example 1.7	5.0% by wt.	-
Hydroxylapatite suspension	-	5.0% by wt.
Example 1.1		
Polywax 1550	2.0% by wt.	2.0% by wt.
Texapon K 1296	1.5% by wt.	1.5% by wt.
Titanium dioxide	1.0% by wt.	1.0% by wt.
Cekol 500 T	1.0% by wt.	1.0% by wt.
Na fluoride	0.33% by wt.	0.33% by wt.
Na benzoate	0.25% by wt.	0.25% by wt.
Aroma	1.0% by wt.	1.0% by wt.
Tagat S	0.2% by wt.	-
Na saccharinate	0.15% by wt.	0.15% by wt.
Trisodium phosphate	0.10% by wt.	0.10% by wt.
Sorbitol	31.0% by wt.	31.0% by wt.
(70% strength in water)		
Water	ad 100% by wt.	ad 100% by wt.

The following commercial products were used:

Plantaren® 1200:

 C_{12} - C_{16} -fatty alcohol oligo-(1.4)-

glucoside about 50% by weight in

water

Manufacturer: HENKEL KGaA

Cremophor® RH 60: 10

Castor oil (hydrogenated) poly(60)-

glycol ether

Manufacturer: BASF

Arlatone® 289:

Castor oil (hydrogenated) poly(54)-

glycol ether

15 Manufacturer: Atlas Chemie (ICI)

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H 3763 PCT/EP99/09683

Synth. amorph. silica, BET 60 m²/g

Tamped density: 350 g/l

Manufacturer: DEGUSSA

Sident® 22 S: Hydrogel silica, BET 140 m²/g

Tamped density: 100 g/l

Manufacturer: DEGUSSA

Polywax® 1550: Polyethylene glycol, MW: 1550

Softening point 45-50°C

Manufacturer: RWE/DEA

10 Texapon® K 1296: Sodium lauryl sulfate powder

Manufacturer: HENKEL KGaA

Cekol® 500 T: Sodium carboxymethylcellulose

Viscosity (2% strength in water,

Brookfield LVF 20°C): 350-700 mPas

Supplier: Nordmann-Rassmann

Tagat® S: Polyoxyethylene-(20) glyceryl monostearate

Manufacturer: Tego Cosmetics

(Goldschmidt)

Patent claims

A suspension of poorly water-soluble calcium salts, 1. phosphates, fluorides and from chosen fluorophosphates, in a liquid medium in which these 5 salts are insoluble or poorly soluble, characterized in that the calcium salts are present in the form of primary particles having diameters of from 5 10 lengths of from and 50 nanometers stabilized against and are 150 nanometers 10 agglomerization by a content of at least 0.01% by weight, based on the weight of the suspension, of a of a water-soluble surfactant or water-soluble polymeric protective colloid.

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- 2. The suspension as claimed in claim 1, characterized in that 1 to 40% by weight of the poorly soluble calcium salts and, for the stabilization, 0.1 to 10% by weight, based on the weight of the poorly soluble calcium salt, of a water-soluble surfactant or of a water-soluble polymeric protective colloid are present in the suspension.
- 2. claimed in claim 1 suspension as 3. for the stabilization, that, characterized in 25 nonionic surfactants are present in an amount of from 1 to 10% by weight, based on the weight of the poorly soluble calcium salt.
- 30 4. A process for the preparation of the suspension as claimed in claim 1-3 by precipitation processes from aqueous solutions of water-soluble calcium salts and aqueous solutions of water-soluble phosphate or fluoride salts, characterized in that the precipitation is carried out in the presence of

water-soluble surfactants or water-soluble polymeric protective colloids.

- 5. A process for the preparation of the suspension as claimed in claim 1-3 by precipitation from an acidic solution of a water-soluble calcium salt and a stoichiometric amount of a water-soluble phosphate salt with a pH below 3 by increasing the pH using aqueous alkalis or ammonia in the presence of water-soluble surfactants or water-soluble polymeric protective colloids.
 - 6. The use of the suspension as claimed in any of claims 1-3 as remineralizing component in compositions for the cleaning and care of teeth.
 - 7. A toothpaste with a content of silica polishing agents, humectants, binders and aromas, characterized in that 0.1-5% by weight of fine calcium salts from the group amorphous calcium phosphate, hydroxylapatite, fluorapatite and calcium fluoride are present in the form of a suspension as claimed in claim 1-3.

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Applicant Authority

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Additional inventors are being named on supplemental sheet(s) attached hereto

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